REMARKS

I. Claims Status

Claims 23, 26, 28, 30-34, 37-40, 44, 46-50, and 57-59 are pending in the application. Claims 52-56 are sought to be cancelled without prejudice to or disclaimer of the subject matter contained therein. Claims 23, 28, 34, 37-40 and 44 are sought to be amended. Support for the amendments can be found in Applicants' specification, for example, at Figures 1(a)-1(c). Support for new claim 59 can be found in Applicants' specification, for example, in original claim 10, in figure 1(c), and on page 5, lines 40-45. These changes are not believed to introduce any new matter, and their entry is respectfully requested.

II. Sequence Listing and Sequence Identification Numbers

The "Brief Summary of the Drawings" section has been amended to correctly correlate novel sequences depicted in the figures with those in the sequence listing. Applicants respectfully request entry of these amendment, which are merely formal in nature and do not constitute new matter.

In addition to the novel sequences provided in the sequence listing, Figure 1a also depicts prior art nucleic acid sequences encoding UreA and B (including a short non-coding region bridging the two encoding sequences) from *Helicobacter felis*, *H. pylori*, and *H. heilmannii*. In addition to the novel sequences provided in the sequence listing, Figure 1b also depicts prior art amino acid sequences of UreA from *Helicobacter felis*, *H. pylori*, and *H. heilmannii*. In addition to the novel sequences provided in the sequence listing, Figure 1c also depicts prior art amino acid sequences of UreB from *Helicobacter felis*, *H. pylori*, and *H. heilmannii*. These prior art sequences are merely provided in the figures to illustrate the relative lack of homology between the genes/proteins according to the invention and those known in the art at the date of filing.

III. Maintained Objections to Claims 37-39 and 44

Claims 37-39 and 44 were objected to for broadening the scope of the claims from which they depended. Office Action, pages 3-4. Applicants have amended these claims and believe

that the objection has been rendered moot. Accordingly, Applicants request that the Examiner reconsider and withdraw the objections raised to claims 37-39 and 44.

IV. Maintained Rejections

A. Enablement Rejection of Claims 46-49 Under 35 U.S.C. §112, 1st ¶

Claims 46-49 are rejected under 35 U.S.C. § 112, 1st ¶ for allegedly failing to comply with the enablement requirement. Office Action, page 5. In particular, the Examiner alleges that

> Numerous factors complicate the ***gene therapy art*** which have not been shown to be overcome by routine experimentation. . . . Therefore, even if the specification . . . [enables] the construction of the gene delivery vehicle comprising a cell targeting element, in the absence of particular guidance, the artisan would have been required to develop *in vivo* and *ex vivo* means of practicing the claimed methods and such development in the nascent and unpredictable ***gene therapy art*** would have been considered to have necessitated undue experimentation on the part of the practitioner.

Id. at pages 5-6 (emphasis added). Applicants strongly traverse the rejection on the grounds that the basis for the rejection is improper.

The enablement rejection of the claims is improper because they have been examined in light of gene therapy art, which is irrelevant to the claimed subject matter. Gene therapy pertains to methods of treating diseases by replacing or supplementing defective or misfunctional genes. Such therapy is principally directed to treating *hereditary* diseases in which a mutant allele is replaced or supplemented with a functioning gene.

In contrast to gene therapy, Applicants' claims 46-49 pertain simply to immunogenic compositions. These claims are limited to compositions capable of eliciting an immune response from a host organism. Such compositions need not provide gene therapy. Rather, such compositions are defined merely by their ability to stimulate an immune response. In the context of the present application, the immunogenic compositions are for stimulating the production of antibodies capable of targeting, *inter alia*, *H. felis* antigens. Hence, the art pertaining to simple DNA vaccination is more pertinent to the claimed subject matter than is art relating to gene therapy. Applicants respectfully assert that art pertaining to simple DNA vaccination provides a

better perspective than art pertaining to gene therapy by which to assess enablement of claims 46-49.

Although some techniques of gene therapy may be shared with the field of DNA vaccination (*e.g.*, transfection and expression of exogenous DNA), the goals and predictability or measures of success for these two fields are very different. Indeed, the field of DNA vaccination is much more developed and mature than the field of gene therapy. There are many successful examples from within the art of DNA vaccination that the skilled artisan can look to for guidance. The field of DNA vaccination is also far more predictable than the field of gene therapy, and generally the former requires less direction or experimentation. Because the art is replete with successful examples of DNA vaccination, the skilled artisan would have no reason to look in the gene therapy art.

For example, Applicants provide herewith Hasan, U. *et al., J. Immunol. Methods 229*:1-22 (1999) (Exhibit A). Table 1 of Hasan *et al.* provides an extensive list describing the successful use of DNA in vaccines for viral, bacterial and parasitic antigens. The use of DNA for treating allergies (also an immunologic problem) is also described.

Applicants also provide herewith Todoroki, I. *et al., B.B.R.C. 277*: 159-163 (2000), Myashita, M. *et al., Vaccine 20*:2336-2342 (2002) and Hatzifoti, C. *et al., Vaccine 22*: 2651-2659 (2004) (Exhibits B, C and D). These three articles specifically show DNA vaccination with *Helicobacter* heat shock protein, *Helicobacter* catalase, and *Helicobacter* urease B. Applicants note that these vaccination experiments followed the procedures described in Hasan *et al.* (Exhibit A), which was published in 1999. Moreover, the DNA constructs in these three papers (Exhibits B-D) were made using techniques well known to the skilled artisan and did not require any undue experimentation. Furthermore, the amount of DNA administered and manner of administration in these vaccination experiments is that which is described by Applicants' specification. See page 9, lines 36 to page 10, line 5.

B. Indefiniteness Rejection of Claims 23, 26, 28, 30-34, 37-40, 44, 46-50 and 57-58 Under 35 U.S.C. §112, 2nd ¶

Claims 23, 26, 28, 30-34, 37-40, 44, 46-50 and 57-58 are rejected for allegedly being indefinite. Office Action, page 6. In particular, the examiner alleges the following:

> The sequences claimed are not limited to the alignments shown but have been defined in the Specification to be determined by "One of the many algorithms suitable for the determination of the level of nucleic acid homology". What the algorithms for determining the nucleic acid molecules included in the scope of what is now claimed is unclear, and the meets and bounds of the claims which recite the terms "homologous" and homology" are still unclear.

Id. at pages 6-7. Applicants respectfully traverse the rejection.

Use of the terms "homologous" or "homology" does not render Applicants' claims indefinite because these terms of art are well understood by the skilled artisan. Moreover, the degree of homology is recited in each claim where the term is used (e.g., 85%, 90%, 94%, 97% etc.). Furthermore, the scientific literature is replete with reportings of nucleotide or amino acid sequences having certain percentage homologies.

Nonetheless, solely to expedite prosecution and not in acquiescence to the rejection, Applicants have amended the claims to refer to the sequence alignment parameters by which the percentage of homology can be ascertained. These parameters provide specific allowed values for sequence mismatches, open gaps or extended gaps. The skilled artisan is generally aware of sequence alignment algorithms and use of parameters to constrain comparative sequence alignments to derive homology values. The skilled artisan is able to select a suitable computer program to use the identified parameters in an algorithm to determine homology. Moreover, Applicants describe such suitable computer programs or algorithms including Align Plus for Windows (available from Scientific and Educational Software, P.O.Box 72045 Durham, N.C. 27722-2045, USA) and "Clustal W," also publicly available. *See* Specification, page 10, lines 38-44.

Hence, the skilled artisan reading Applicants' claims understands that the specific percentage homology can be determined using the parameters identified in the appropriate figure,

which are parameters of publicly available sequence alignment algorithms. Because such algorithms are publicly available, any skilled artisan could obtain copies and utilize them to ascertain whether a particular sequence has the requisite homology to fall within the scope of the claims. Accordingly, Applicants request that the Examiner reconsider and withdraw the indefiniteness rejection of claims 23, 26, 28, 30-34, 37-40, 44, 46-50 and 57-58.

C. Rejections Under 35 U.S.C. § 102(b)

The Examiner has maintained or issued a rejection of claims 23, 26, 28, 30-34, 37-40, 44, 46-50 and 57-58 under 35 U.S.C. § 102(b) for allegedly being anticipated by Labigne *et al.* (U.S. Pat. No. 5,843,460). Solely to expedite prosecution and not in acquiescence to the rejection, Applicants have amended the claims to clarify the meaning of homology. The claims are now restricted to i) nucleotide or peptide sequences having the requisite homology as defined using the recited algorithmic parameters in an alignment against the *entire length* of the recited SEQ ID NO. (i.e., a global alignment), or ii) a 70 nucleotide or amino acid long stretch of such a sequence. Applicants respectfully point out that any 70 nucleotide or amino acid long stretch of such sequences will also necessarily have the requisite homology as defined using the recited algorithmic parameters.

Since Labigne *et al.* fails to disclose such sequences, Applicants believe that this rejection is now moot and respectfully request the Examiner to reconsider and withdraw the rejection.

V. New Grounds of Rejections

A. Written Description Rejection Under 35 U.S.C. §112, 1st ¶

Claims 1-27 are rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. Office Action, page 11. In particular, the Examiner states that "parts or regions of SEQ ID NO 1, 2 and 3 . . . chosen to be . . . [a part] of the claimed nucleic acid and polypeptides . . . [have] not been described, nor have the recombinant genes used to produce a plurality of protein forms of homologous urease XY, other than those shown in Figure 1a . . . been described." *Id.* The Examiner also alleges that "[t]he

claimed nucleic acid sequences and polypeptides are required to have . . . a sequence that encodes or has an antigenic functional characteristic to Helicobacter felis ureaseXY, but the antigenic/immunogenic region of Helicobacter felis urease XY has not been described by any specific monoclonal antibody, or to have any specific chemical structure, but only to comprise any region of the sequence that can be incorporated into a larger molecule and be reactive with any antibody reactive with Helicobacter felis ureaseXY." *Id.* at page 12. The Examiner also states that "[t]he claimed nucleic acids and polypeptides that comprise sequences other than those set forth in Figure 1a, SEQ ID NO 1, 2 or 3, and only comprise an antigenic epitope of 3-10 amino acids out of a possible 700+ amino acids fail to have an adequate written description in the instant specification." *Id.* at page 12.

Applicants respectfully point out that claims 1-22 in the captioned application are cancelled. Moreover, to the extent this rejection relates to the pending claims, Applicants respectfully assert that the claims have been amended to clarify the meaning of homology and that parts or fragments must be at least 70 nucleotides or amino acids long.

Furthermore, Applicants' specification provides an adequate written description of the claimed parts or fragments for the skilled artisan:

> When a polypeptide is used for e.g. vaccination purposes or for raising antibodies, it is however not necessary to use the whole polypeptide. It is also possible to use a fragment of that polypeptide that is capable, as such or coupled to a carrier such as e.g. KLH, of inducing an immune response against that polypeptide, a so-called immunogenic fragment. An "immunogenic fragment" is understood to be a fragment of the full-length polypeptide of the structural subunit X or Y, that still has retained its capability to induce an immune response in the host, i.e. comprises a B- or T-cell epitope. At this moment, a variety of techniques is available to easily identify DNA fragments encoding antigenic fragments (determinants). The method described by Geysen et al (Patent Application WO 84/03564, Patent Application WO 86/06487, U.S. Pat. No. 4,833,092, Proc. Natl Acad. Sci. 81: 3998-4002 (1984), J. Imm. Meth. 102, 259-274 (1987), the so-called PEPSCAN method is an easy to perform, quick and well-established method for the detection of epitopes; the immunologically important regions of the polypeptide. The method is used world-wide and as such well-known to man skilled in the art. This (empirical) method is especially suitable for the detection of B-cell epitopes. Also, given the

> sequence of the gene encoding any protein, computer algorithms are able to designate specific polypeptide fragments as the immunologically important epitopes on the basis of their sequential and/or structural agreement with epitopes that are now known. The determination of these regions is based on a combination of the hydrophilicity criteria according to Hopp and Woods (Proc. Natl. Acad. Sci. 78: 38248-3828 (1981)), and the secondary structure aspects according to Chou and Fasman (Advances in Enzymology 47: 45-148 (1987) and U.S. Pat. No. 4,554,101). T-cell epitopes can likewise be predicted from the sequence by computer with the aid of Berzofsky's amphiphilicity criterion (Science 235, 1059-1062 (1987) and U.S. patent application NTIS U.S. Ser. No. 07/005,885). A condensed overview is found in: Shan Lu on common principles: Tibtech 9: 238-242 (1991), Good et al on Malaria epitopes; Science 235: 1059-1062 (1987), Lu for a review; Vaccine 10: 3-7 (1992), Berzowsky for HIV-epitopes; The FASEB Journal 5:2412-2418 (1991).

Specification page 6, line 32 to page 7, line 8. Hence, the skilled artisan would understand upon reading the specification that Applicants were in possession of the full scope of the claimed invention, including the claimed parts or fragments.

Accordingly, Applicants believe that this rejection is now moot and respectfully request the Examiner to reconsider and withdraw the rejection.

B. Rejections Under 35 U.S.C. § 112, 2nd ¶

1. Claims 1-20

Claims 1-20 are rejected under 35 U.S.C. § 112, 2nd ¶ for allegedly being indefinite. In particular, the Examiner states that "[c]laims 1-20 recited the phrase 'comprising regions which act as antigens specific to Helicobacter pylori'. Office Action, page 13.

Applicants respectfully point out that claims 1-20 were previously cancelled. Moreover, none of the claims recite the above quoted phrase. Hence, Applicants believe that this rejection is moot, and respectfully request that it be reconsidered and withdrawn.

2. Claim 39

Claim 39 is rejected for insufficient antecedent basis. Office Action, page 14. Claim 39 has been amended thereby rendering the rejection moot. Applicants respectfully request that the

rejection be reconsidered and withdrawn.

C. Rejections Under 35 U.S.C. §101

The Examiner indicates that "[c]laims 23, 26 and 28 are not directed to isolated and purified nucleic acid molecules and therefore do not show the hand of man; the claimed invention is directed to non-statutory subject matter. The rejection could be obviated by amending the claims to recite ------isolated and purified-----." Office Action, page 14.

Applicants thank the Examiner for suggesting claim language to overcome the rejection. Solely to expedite prosecution and not in acquiescence to the rejection, Applicants have amended claim 23 and believe that the rejection is now moot. Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

D. Rejections Under 35 U.S.C. § 102(b)

Claims 23, 26, 28, 30, 33, 34, 37-39, 40, 44, 57 and 58 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gootz *et al.* (1994). Office Action, page 14. Solely to expedite prosecution and not in acquiescence to the rejection, Applicants have amended the claims to clarify the meaning of homology. The claims are now restricted to i) nucleotide or peptide sequences having the requisite homology as defined using the recited algorithmic parameters in an alignment against the *entire length* of the recited SEQ ID NO. (i.e., a global alignment), or ii) a 70 nucleotide or amino acid long stretch of such a sequence. Applicants respectfully point out that any 70 nucleotide or amino acid long stretch of such sequences will also necessarily have the requisite homology as defined using the recited algorithmic parameters.

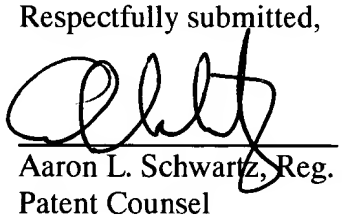
Since Gootz *et al.* fails to disclose such sequences, Applicants believe that this rejection is now moot and respectfully request the Examiner to reconsider and withdraw the rejection.

CONCLUSION

Applicants do not believe that any other fee is due in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. 02-2334. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. 02-2334.

Applicants submit that this application is in condition for allowance, and request that it be allowed. The Examiner is requested to call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,



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